REMARKS

Claims 9 and 11 are in this application. Claim 9 has been amended.

The examiner rejects Claims 9 and 11 as lacking novelty in view of US 6,231,536. This is respectfully traversed.

US 6,231,536 is directed to a treatment method for cancers with ultrapheresis procedures to stimulate the patient's immune system to attack solid tumors. However, the citation does not specifically disclose or teach the use of thalidomide in the treatment of hepatocellular carcinoma with a specific amount of 30 to 1200mg. Furthermore, the Applicant has further limited the term "comprising" in the first line of Claim 9 to "consisting of" so that the claimed method merely includes a single administration step. The applicants disagree respectfully with the Examiner's statement that the cited prior art discloses in column 8, example 4 that thalidomide is administered alone to the subject. According to Example 4 of the citation, a patient with metastic adenocarcinoma was treated with 15 ultrapheresis procedures and thalidomide. According to the '536 patent the treatment of adenocarcinoma results from the ultrapheresis in combination with thalidomide rather than thalidomide *per se* only. Therefore, the method of treating hepatocellular carcinoma claimed in this application is not the same as that of the '536 patent. Anticipation requires that each and every element of the claimed invention be disclosed in a single prior art reference. *In re Paulsen*, 30 F.3d 1475, 31 USPQ 1671 (Fed. Cir. 1994). For anticipation, there must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention. *Scripps Clinic & Res. Found. v. Genentech, Inc.*, 927 F.2d 1565, 18 USPQ2d 1001 (Fed. Cir. 1991). Since there is clearly a difference between amended Claim 9 and the disclosure of the '536 patent which requires both thalidomide and ultrapheresis, Claims 9 and 11 are not anticipated by the reference. Therefore, it is respectfully requested that the rejection be withdrawn.

The examiner rejects Claims 9 and 11 as being obvious in view of US 5,629,327, Masiero *et al.*, US 5,696,092 and Aarestrup *et al.* This is respectfully traversed.

The Applicant respectfully disagrees with the examiner's opinion. The present invention relates to the use of thalidomide *per se* for treating hepatocellular carcinoma in a specific amount of 30 to 1200mg. Examples 2 and 3 illustrate a thalidomide treatment with 100mg to patients having hepatocellular carcinoma, and show that oral administration of a capsule containing thalidomide as a single principle ingredient significantly reduces the tumor size and/or the serum level of alpha-fetoprotein in the patients.

US 5,629,327 is directed to a group of compounds (including thalidomide) having anti-angiogenesis activity. The citation illustrates the use of thalidomide in the treatment of corneal neovascularization and suggests some diseases involving undesired angiogenesis, such as rheumatoid and hemangiomas, treatable by thalidomide. However, the citation does not specifically disclose or teach the use of thalidomide in the treatment of hepatocellular carcinoma with a specific amount of 30 to 1200mg. Since no examples of solid tumors are given in the citation and there is no specific disclosure concerning the use of thalidomide to treat hepatocellular carcinoma in the citation, the citation does not provide one with a reasonable expectation of success that thalidomide can be used to treat hepatocellular carcinoma.

Masiero *et al.* discloses that thalidomide is currently tested in phase II of clinical trials for prostate cancer, glioblastoma and breast cancer. However, the citation does not suggest or imply the treatment of hepatocellular carcinoma by 30 to 1200mg of thalidomide as emphasized in the present invention. It is well known in the art that the treatment of a type of cancer does not mean that the same treatment will work for all types of solid tumors. As shown in the article previously submitted (Paragraph 9 of the article obtained from the website www.netwellness.com/healthtopics /cancer/solid.cfm), some tumors of the

breast, uterus and prostate grow faster in the presence of certain hormones. Based on the teachings of the article, because of the differences in sensitivity to sex hormones of the breast and prostate hormones, the disclosures in Masiero of treatment of breast and prostate cancer do not teach treatment of hepatocellular carcinoma with a specific amount of 30 to 1200mg.

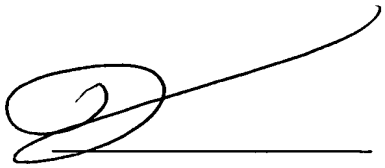
US 5,696,092 focuses on the use of compounds that inhibit arachidonic acid released by cells of a tumor for preventing metastasis of the tumor. The citation teaches that additional therapeutic agents such as angiogenesis inhibitors can be used in combination with the arachidonic acid release inhibitors, but does not provide any hint concerning the treatment of hepatocellular carcinoma by using thalidomide in a specific amount of 30 to 1200mg as disclosed in the invention.

Aarestrup *et al* discloses the treatment of liver granulomas with 30mg of thalidomide. It is known in the art that liver granulomas is different from hepatocellular carcinoma. For example, as shown in the article "Annuals of Contemporary Diagnostic Pathology 1998, Volume 2, pp.79-93,"(see Attachment) granulomas may be found in the liver, especially in conjunction with Hodgkin's disease, sarcoidosis, and tuberculosis and the neoplastic hepatocytes in HCC display the usual cytologic features of malignancy . Since the hepatocellular carcinoma is distinguishable form the liver granulomas, the disclosures of Aarestrup in combination with US patent 6,231,536 do not provide motivation to persons skilled in the art to derive the treatment of hepatocellular carcinoma with thalidomide in a specific amount of 30 to 1200mg as disclosed in the invention.

Given the above, the above-mentioned citations, either alone or in combination, cannot render the invention obvious. The rejections under 35 USC 103 should be withdrawn.

Accordingly it is respectfully submitted that the present application is in condition for allowance and favorable consideration is respectfully requested.

Respectfully submitted,



JANET I. CORD
LADAS & PARRY
26 WEST 61ST STREET
NEW YORK, NEW YORK 10023
REG. NO.33778 (212)708-1935